

IN THE SUBSTITUTE SPECIFICATION

Please replace paragraph [0005] as follows:

In this situation, there are some reports that a soybean Kunitz-type trypsin inhibitor disclosed in Japanese Patent - Publication No. 121869/1995 and a vascular endothelial cell growth factor/vasopermeable factor antagonist disclosed in Japanese Patent Laid-Open No. 245347/1998 have an effect of suppressing accumulation of body fluid to prevent decline of the physical strength of patients and to enhance therapeutic effect. In the case of lactoferrin as mentioned above, an example in which a peptide derived from lactoferrin is used as an agent for suppressing inflammation caused by an endotoxin (lipopolysaccharide (LPS)) derived from gram-negative bacteria is disclosed in Japanese Patent Laid-Open No. 165248/1996. Another example in which lactoferrin per se is used in combination in treatment for diseases induced by the endotoxin is disclosed in Japanese Patent Laid-Open No. 114675/1998. It has never been examined, however, whether lactoferrin can be used to alleviate the exudation of plasma albumin ~~or body fluid~~ at the inflammatory site or the increase of blood neutrophils.

Please replace paragraph [0007] as follows:

Brief Description of the Drawings

Fig. 1 shows an effect of human-type lactoferrin on reducing the concentration of albumin contained in the lavage-fluid of an abdominal cavity 5 hours after administration of lipopolysaccharide (LPS).

Fig. 2 shows an effect of human-type lactoferrin on inhibiting increase of the number of blood neutrophils 5 hours and 24 hours after administration of LPS.

Fig. 3 shows an improved effect of human-type or bovine-type lactoferrin on exudation of albumin in the abdominal cavity in the inflammation induced by LPS.

Fig. 4 shows comparatively an inhibitory effect of human-type or bovine-type lactoferrin on the plasma TNF α production in the inflammation induced by LPS.

Fig. 5 shows an effect of human-type lactoferrin on decreasing the amount of ascites accumulated in the abdominal cavity 5 hours after administration of LPS.

Fig. 6 shows a clear effect of the ~~injection~~ administration time of lactoferrin on the effect of decreasing accumulation of albumin induced by LPS.

Fig. 7 shows the difference in the administration route of lactoferrin on the effect of decreasing accumulation of albumin induced by LPS in the peritoneal cavity.

Please replace paragraph [0011] as follows:

The product of the invention was evaluated by confirming the in vivo effect in an animal experiment using rats. As a result, it was confirmed that administration of human-type lactoferrin reduced both accumulation of albumin that was exuded in the abdominal cavity and decline of blood albumin concentration caused by inductivity of LPS administered in the abdominal cavity, and greatly suppressed the symptoms such as increase of neutrophils caused by inflammation. In the invention, a variety of pharmaceutical formulations containing human-type lactoferrin may be administered to a patient or immune insufficient subject to whom an inflammatory disease such as sequela sepsis is possibly expected to develop. Thus, it has become first possible to utilize an agent containing human-type lactoferrin as an effective ingredient in order to suppress exudation of albumin at the inflammatory region or decrease maintain blood albumin concentration, hasten recovery of a usual level of blood neutrophils, and suppress increase of neutrophils.

Please replace paragraph [0020] as follows:

Example 4

Study on the effect of difference of the ~~injection~~ administration time of human-type lactoferrin on alleviation of symptoms (accumulation of albumin in the abdominal cavity) resulting from inflammation induced by LPS

Test Method: In this test method, lactoferrin was administered 18 hours or 15 minutes before or 60 minutes after administration of LPS. Otherwise, the test was carried out in the same manner as in Example 1.

DISCUSSION OF THE AMENDMENT

The substitute specification has been amended to address the objection at paragraph 3 of the Office Action.

No new matter is believed to have been added by the above amendment. Claims 9-32 remain pending in the application.